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THE EFFECT OF PROLONGED BODILY INACTIVITY ON CARBOHYDRATE TOLERANCE

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16. Abstract The influence of prolonged bodily inactivity on carbohydrate tolerance was investigated. Prednisone-glucose-tolerance tests were conducted at 4-week intervals on 20 patients confined to bed for at least 8 weeks because of diseases known not to have any direct influence on carbohydrate metabolism. In two cases, the patients were re-examined 2 years after remobilization. The following results were obtained: 1) Reductions in carbohydrate tolerance can be brought about by prolonged bodily inactivity alone. 2) The more complete the immobilization, and the longer it lasts, the greater the impairment of carbohydrate metabolism. 3) Carbohydrate tolerance reductions due to confinement in bed are observed almost exclusively in older persons. 4) As a rule, these disturbances of carbohydrate metabolism are reversible after remobilization.

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THE EFFECT OF PROLONGED BODILY INACTIVITY ON CARBOHYDRATE TOLERANCE

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Impairment of carbohydrate tolerance has been observed and /814** described recently as a consequence of a great variety of diseases, e.g. in connection with cardiac infarction (Frehner and Wegmann, Reaven et al., Braunsteiner et al., Cohen and Shafrir, Magyar and Krutsay), vasculopathies (Thiele, Vitelli et al.), degenerative arthropathies (Escofet and Quercol), carcinoma of the cervix uteri (Cheraskin et al.), and tuberculosis (Mücke and Pfaffenberg). The cause has usually been presumed to be a diabetes-promoting influence of the primary disease. Only in specific cases has it been considered that bodily inactivity could play a role, either as a supplementary factor (Bibergeil, Conn and Fajans, Goto et al.) or even as a crucial factor by itself.

Therefore, the objective of the present investigation will be to ascertain whether bodily inactivity -- in the form of bed rest -- can by itself impair the carbohydrate tolerance.

Material and Method

The patients selected for study in this investigation were ones who had been confined to bed for long periods by diseases known to have no direct influence on carbohydrate tolerance. The following were selected:

Nine patients with surgical diseases: fractures of the neck of the femur, pertrochanteric fractures, tibia fractures; seven patients with orthopedic diseases: scolioses, exostoses, amputations,

*The results in this work come from an inaugural dissertation by R. Frenzel (Dresden 1968).

**Numbers in the margin indicate pagination in the foreign text.

myelodysplasia, and four patients with ulcus cruris.[1]

Patients with adiposity and diabetes mellitus in their heredity were excluded from the experiments.

Carbohydrate tolerance was to be tested with a technique which was as sensitive as possible. Among the numerous alternatives, oral double administration of dextrose after sensitization with prednisone (Bibergeil's procedure) was selected: The subject received 20 mg prednisone orally at 11:30 p.m. on the eve of the experiment, and the same amount at 6:00 a.m. on the morning of the day of the experiment. Starting at 8:00 a.m., the subject then received in the usual fashion two Staub-Traugott doses of 50 g glucose 90 min apart. Blood sugar was determined at half-hour intervals until 240 minutes after the beginning of the experiment. Urine was checked in the morning, after 60 min, and after 150 min with Biophan test paper. If the enzyme-soaked test strip turned green, urinary sugar was indicated. The quantitative content was determined in the polarimeter.

The experiment was repeated with every patient at 4-week intervals, employing the same method, as long as the patient was under clinical treatment. In all, 20 subjects were tested in this manner. With two subjects, the testing was repeated with the same method about 2 years after remobilization.

Since in this modification of the prednisone-glucose-tolerance

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[1]The subjects were under treatment in the following clinics: Surgical Clinic (Head physician: Dr. H.D. Schumann) of the District Hospital of Dresden-Friedrichstadt, Orthopedic Clinic (Director: Dr. H. Büschelberger) of the Medical Academy of Dresden, Skin Clinic (Head physician: Dr. H. Hering) of the District Hospital of Dresden-Friedrichstadt. We are grateful to the directors of these clinics for permission to conduct the studies.

test (PGTT), normal values have not yet been established, a normal range itself must be delineated. As a control group, 27 presumably metabolically healthy hospital patients from different wards were employed who were immobilized, if at all, only briefly. Selection was arbitrary. From the test results, the normal range was established by twice the standard deviation from the mean-value curve. This was done separately for subjects up to 50 years old (eight cases) and for those over 50 (19 cases). The normal range (for the older subjects) found in this way agreed well with that established by Bibergeil. The t-test (Student) was employed as a statistical verification procedure.

Blood sugar was determined enzymatically. All analyses were performed by the same investigator (Frenzel). Initially, double determinations were undertaken. However, since the error in the method was only 3.41%, double determinations were dispensed with in the further course of the studies.

The external experimental conditions were the same for all test subjects and members of the control group.

Results

In view of the known relationship between carbohydrate tolerance and age, the results of the studies were analyzed separately for two groups: first, the subjects who had not yet completed their 50th year at the time of the testing (7), and second, the subjects who were 50 years old and older (13).

The following was found: In the group of the younger subjects, (up to 50 years old), only one of seven patients exhibited any impairment of carbohydrate tolerance in the course of prolonged inactivation (after 10 weeks), and this impairment was only minor. /815

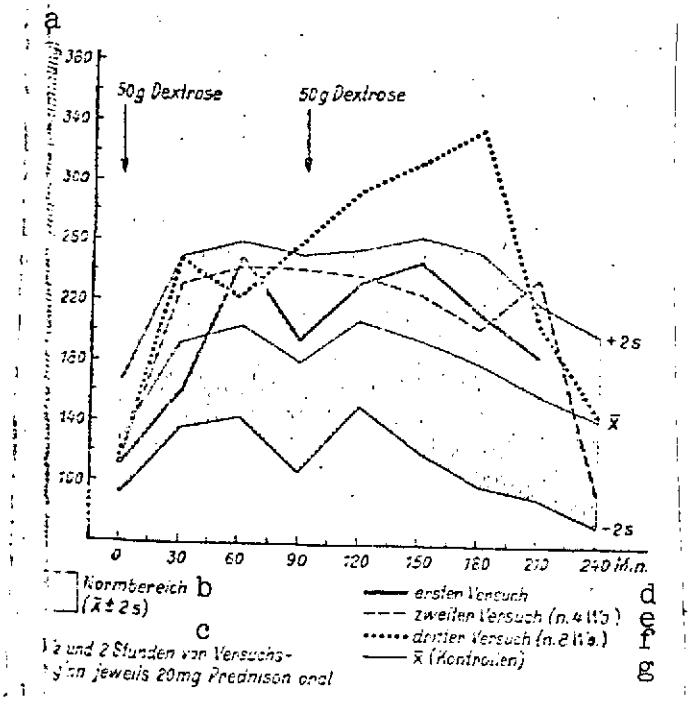

Fig. 1. Repeated prednisone-glucose tolerance tests during prolonged confinement in bed. Marie Sch--, 64-year-old patient with medial fracture of the neck of the right femur. Height: 158 cm. Weight: 49.0 kg. No diabetes mellitus known in the family, no diabetes symptoms. Gradual, moderate impairment of carbohydrate tolerance during bed rest.

Key: a. mg blood sugar per 100 ml plasma (enzymatic determination).
b. Normal range
c. 8 1/2 and 2 hours before beginning of experiment, 20 mg prednisone orally in each case
d. First experiment
e. Second experiment (after 4 weeks)
f. Third experiment (after 8 weeks)
g. Controls

On the other hand, among the 13 patients over 50, a marked decrease in carbohydrate tolerance was found for six of them after they had been confined to bed for 8 weeks. Figure 1 shows an example.

One 81-year-old patient exhibited a pathological behavior after just the first dose (Fig. 2). Starting from a blood sugar of 182 mg-%, the test curve rose to a maximum of 454 mg-%. The repetitions of the tests after 4 and 8 weeks of strict confinement to bed yielded curves of increasingly diabetic character. Glycosuria was regularly found after the test, but otherwise only in traces. Two years after release from the hospital and remobilization, a control study was carried out with the same method: The carbohydrate tolerance was considerably improved. While the blood sugar curve was substantially lower than in the first test, it was still not entirely in the normal

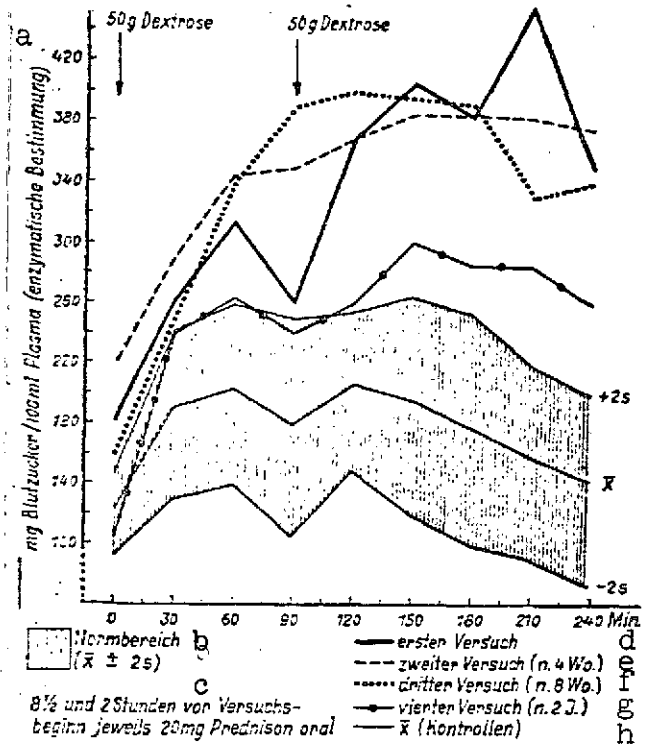

Fig. 2. Repeated prednisone-glucose tolerance tests during prolonged confinement in bed and after remobilization. Thekla O--, 81-year-old female patient with fracture of neck of right f e m u r. Height: 158 cm, Weight: 48.0 kg. No diabetes mellitus known in the family, no diabetes symptoms. Pathological t e s t curve immediately after beginning of confinement to bed. Extensive normalization 2 years after remobilization.

Key: a-g. Same as Fig. 1.
h. Fourth experiment (after 2 years)

normal range (initially, 105 mg-%); maximum 302 mg-%). In this single case, we probably detected an asymptomatic diabetes, which experienced a temporary tolerance impairment due to the confinement in bed.

Statistical verification of these results (00) comes up against difficulties associated with the method. It is superfluous for the group of younger subjects, in whom there was only one case with a minor impairment of carbohydrate tolerance.

Taking the entire group of 13 older subjects together, no significant differences between the test results before and after 8 weeks of bed rest can be ascertained. Only when the six patients with marked impairment of carbohydrate tolerance are considered separately can significant differences be discovered: For these six patients, the averaged blood-sugar values from the first dose were compared (individually) with those from the third dose after at least 8 weeks bed rest, and checked with the aid of the t-test. In this way, based on an error probability of $p < 0.05$, significant differences were obtained for the blood-sugar values from

the third dose (after 8 weeks) 90, 120, 150, and 180 min after the start of the experiment as compared with the corresponding values from the first administration. For the 120-min value, p was actually less than 0.005.

In a closer examination of these six patients with demonstrable impairment of carbohydrate tolerance, we were struck by the fact that they were all persons confined to bed with extensive plaster casts or traction bandages, and were thus completely immobilized. Many of them (e.g. with ulcus cruris or orthopedic complaints) still had some small degree of freedom of movement, and were able to leave bed.

The total group of 20 subjects was therefore (ignoring age) divided into two groups, by whether they were completely (9 patients) or only partially immobilized (11 patients). In the same type of testing with the aid of the t-test, significant differences were obtained between the nature of the blood-sugar curves before and after prolonged inactivation only for the group of completely immobilized patients, but not for the group with only partial confinement. In particular, $p < 0.05$ for the 90-, 120-, and 180-min values in the group of nine completely immobilized patients. /816

To investigate the extent to which impairments of carbohydrate tolerance resulting from inactivation are reversible after remobilization, we subsequently attempted to re-examine the patients. We were able to perform another PGTT with the same method on two subjects 2 years after their release from the hospital and remobilization. In one case, normalization of carbohydrate tolerance was complete, and in the second case (Fig. 2), a high degree of normalization was attained.

Discussion of the Results

The results of our studies show that bodily inactivity by itself can result in an impairment of carbohydrate tolerance. To this extent, our findings are in agreement with the experiences of Blotner and Bühr. In addition, it was found that prolonged bed rest did not bring about a reduction in the carbohydrate tolerance in every patient. Declines in tolerance were noted almost exclusively in older persons (over 50). Furthermore, the more complete the confinement and the longer it lasted, the more marked the reductions in tolerance were. From the fact that we observed clear reductions in carbohydrate tolerance in six of nine patients confined completely to bed, it must be concluded that impairment of carbohydrate metabolism must be anticipated in the majority of cases when older persons must be largely immobilized for long periods of time.

Just this frequency of impairment of carbohydrate tolerance due to protracted inactivity is evidence that the patients concerned were not exclusively prediabetics in which the inactivity provoked the manifestation of the diabetes. Naturally, this can occur. Among our cases is an (81-year-old) female patient with a fracture of the neck of the femur, in whom 8 weeks of bed rest produced a pronounced diabetic metabolism situation with glycosuria and blood sugar peaks up to 374 mg-%.

The reversibility of the changes in metabolism which we found, and which had already been found by Bühr, is further evidence that most of the cases were transitory functional disturbances in carbohydrate metabolism. Their appearance is not linked with the existence of a genetic disposition toward diabetes mellitus, and their detection does not justify a diagnosis of prediabetes, latent diabetes, or asymptomatic diabetes.

These conclusions should be kept in mind when disturbances of carbohydrate tolerance are detected in patients with various diseases who are partially or largely confined to bed. In the past, too far-reaching consequences have been drawn in such cases, namely by:

1. prematurely diagnosing a "genuine" asymptomatic diabetes, when it is really just a matter of a temporary, functional carbohydrate metabolism disturbance, and by
2. postulating direct causal relationships between some primary disease and diabetes mellitus, without taking sufficient account of the possibilities of an impairment of carbohydrate metabolism due to the bodily immobilization enforced by the primary disease.

There remains the question of how bodily inactivity can lead to impairment of carbohydrate tolerance. Several possibilities are conceivable, and have been discussed: first, disturbance of peripheral utilization of glucose as a consequence of inactivation of the musculature (Bühr, Dulin and Clark) or as a consequence of retarded blood circulation, reduced oxygenation of the blood, which can weaken the action of insulin (Gardiner, Martin and Young). On the other hand, it can be imagined that the restriction of metabolism during prolonged immobilization can also result in inactivation of the pancreas, which then is no longer able to react adequately to strong functional stimuli (such as presented in a PGTT). In physiological atrophy of the pancreas due to aging (Bürger, Ritter), the cause must be sought for the fact that reductions in carbohydrate tolerance appear earlier and more intensely in old bed-ridden persons. Our own investigations do not supply any important contributions toward a solution of this problem. Hence, we dispense with a detailed discussion at this point.

Summary

The influence of prolonged bodily inactivity on carbohydrate

tolerance was investigated. Prednisone-glucose-tolerance tests were conducted at 4-week intervals on 20 patients confined to bed for at least 8 weeks because of diseases known not to have any direct influence on carbohydrate metabolism. In two cases, the patients were re-examined 2 years after remobilization.

The following results were obtained:

1. Reductions in carbohydrate tolerance can be brought about by prolonged bodily inactivity alone.

2. The more complete the immobilization, and the longer it lasts, the greater the impairment of carbohydrate metabolism.

3. Carbohydrate tolerance reductions due to confinement in bed are observed almost exclusively in older persons.

4. As a rule, these disturbances of carbohydrate metabolism are reversible after remobilization.

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